

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT REISSUE application of:

Patentees: Yong Wei, et al.

U.S. Patent No.: 5,681,589

Reissue
Application No.: TBD

Issued: October 28, 1997

For: LIPOSOMAL CERAMIDE-RELATED COMPOUNDS AND THE
THERAPEUTIC USE THEREOF

Docket No. TLC -144C RIS

Hon. Commissioner of Patents
and Trademarks
Washington, DC 20231

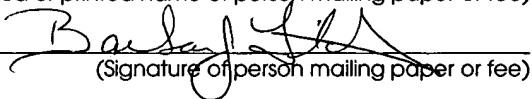
"Express Mail" mailing label number EJ230191851US

Date of Deposit October 27, 1999

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" Service under 37 CFR 1.10 on the date indicated above and addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on October 27, 1999

Barbara J. Fitch

(Typed or printed name of person mailing paper or fee)


(Signature of person mailing paper or fee)

ASSENT OF ASSIGNEE TO REISSUE

The undersigned states that she/he is empowered to execute this Assent on behalf of THE LIPOSOME COMPANY, INC., assignee of the entire interest in United States Patent No. 5,681,589 and hereby assents to the above-identified reissue application. An assignment from the inventors was recorded in the United States Patent and Trademark Office on June 23, 1995 at Reel 7579, Frame 0405. The undersigned certified that to the best of assignee's knowledge and belief, title is in the assignee seeking to take this action.

I declare under penalty of perjury under the laws of the United States of America
(28 U.S.C. § 1746 and M.P.E.P. 602) that the foregoing is true and correct.

Respectfully submitted,

THE LIPOSOME COMPANY, INC.



Michael McGrane
Vice President, General Counsel,
and Secretary

Date: October 25, 1999

052207-46962460

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group Art Unit: 1615

Examiner: Gollamudi S. Kishore

In re PATENT REISSUE APPLICATION of:

Patentees : Yong WEI et al.)
U.S. Patent No. : 5,681,589)
Issued : October 28, 1997)
Reissue)
Application No. : TBD)
Reissue Filed :)
For : LIPOSOMAL CERAMIDE-RELATED)
COMPOUNDS AND THE)
THEREAPUETIC USE THEREOF)
Attorney Docket : TLC 144C RIS)

**DECLARATION AND
POWER OF ATTORNEY**

Date:

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

We, Yong Wei, Eric Mayhew, Imran Ahmad and Andrew S. Janoff, DECLARE:

That we are citizens of the People's Republic of China, United Kingdom, India, and the United States, respectively, and that our post office addresses are, respectively:

Yong Wei, 39 Seneca Trail, Branchburg, NJ 08876

Eric Mayhew, 3905 West Bertuna Street, Seattle, WA 98199

Imran Ahmad, 2408 Fox Run Drive, Plainsboro, NJ 08536

Andrew S. Janoff, 560 Countess Drive, Yardley, PA, 19067, US

That we verily believe ourselves to be the original, first and joint inventors of the invention LIPOSOMAL CERAMIDE-RELATED COMPOUNDS AND THE THERAPEUTIC USE THEREOF described and claimed in the United States Letters Patent No. 5,681,589 issued October 28, 1999 on application no. 545,164, filed October 19, 1995;

That we have reviewed and understood the contents of the reissue specification including the claims.

That we acknowledge our duty to disclose information of which we are aware which is material to the examination of this application under Rule 56(a);

We verily believe that the original United States Letters Patent No. 5,681,589, referred to above, is wholly or partly inoperative because the patentees claimed less than they had a right to claim. The specific errors relied upon are the failure to present the following claims:

16. A compound having the formula $R^1-Y^1-CHZ^1-CH(NY^2Y^3)-CH_2-Z^2$, wherein:

R^1 is a straight-chained alkyl, alkenyl or alkynyl group having from 5 to 19 carbon atoms in the aliphatic chain;

Y^1 is $-CH=CH-$, $-C\equiv C-$ or $-CH(OH)CH(OH)-$;

Z^1 is OH or a phosphorylcholine attachment-inhibiting group selected from the group consisting of $-X^1$, $-OX^1$, $-X^2X^3$ and $-OX^2X^3$;

Y^2 is H, a phenyl group, an alkyl-substituted phenyl group having from 1 to about 6 carbons in the alkyl chain, or an alkyl chain having from 1 to 10 carbons;

Y^3 is H or a group having the formula $-C(O)R^2$ or $-S(O)_2R^2$;

R^2 is a straight-chained alkyl moiety selected from the group consisting of $-(CH_2)_3CH_3$, $-(CH_2)_5CH_3$, $-(CH_2)_7CH_3$ and $-(CH_2)_9CH_3$, an alkenyl group having from 1 to 23 carbon atoms in the aliphatic chain and an alkynyl group having from 1 to 23 carbon atoms in the aliphatic chain;

Z^2 is OH or a phosphorylcholine attachment-inhibiting group selected from the group consisting of $-X^1$, $-OX^1$, $-X^2X^3$ and $-OX^2X^3$;

X^1 is selected from the group consisting of $-C(O)H$, $-CO_2H$, $CH_3C(CH_3)_3$, $Si(C(CH_3)_3)_3$, $Si(PO_4)_2C(CH_3)_3$, a phenyl group, an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino group, a fluorine, a chlorine, and a group having the formula $C(R^3R^4)OH$;

X² is selected from the group consisting of CH₂-, C(CH₃)₂-, Si(PO₄)₂-, Si(CH₃)₂-, SiCH₃PO₄-, C(O)- and S(O)₂-;

X³ is selected from the group consisting of -C(O)H, -CO₂H, -CH₃, -C(CH₃)₃, -Si(CH₃)₃, -SiCH₃(C(CH₃)₃)₂, -Si(C(CH₃)₃)₃, -Si(PO₄)₂C(CH₃)₃, a phenyl group, an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino moiety, a chlorine, a fluorine, or a group having the formula C(R³R⁴)OH, wherein each of R³ and R⁴ is independently an alkyl chain having from 1 to 6 carbons, a phenyl group or an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain;

wherein when Z² is an amino group, R² is an aliphatic chain having from 1 to 9 or from 19 to 23 carbon atoms in the aliphatic chain.

17. The compound of claim 16, wherein R² is an alkyl chain.

18. The compound of claim 16, wherein R¹ is CH₃(CH₂)₁₂-.

19. The compound of claim 16, wherein Y¹ is -CH=CH-.

20. The compound of claim 16, wherein Y² is H.

21. The compound of claim 16, wherein Y³ is -C(O)R².

22. The compound of claim 16, wherein Z¹ is OH.


23. The compound of claim 22, wherein Z² is a group having the formula -X²X³ or -O-X²X³.

24. The compound of claim 23, wherein Z² is -OC(O)CH₃, -OC(O)CH₂CH₂CH₃, -OC(O)CH(CH₃)CH₃, or -OSi(CH₃)₂C(CH₃)₃.

25. The compound of claim 24, wherein Z² is -OSi(CH₃)₂C(CH₃)₃.

26. The compound of claim 22, wherein Z^2 is a group having the formula $-X^1$ or $-OX^1$.
27. The compound of claim 16 having the formula $CH_3(CH_2)_{12}-CH=CH-CH_2Z^1-$
 $CH(NHY^3)-CH_2-Z^2$.
28. The compound of claim 27, wherein Z^1 is OH and Y^3 is a group having the formula $-C(O)R^2$.
29. The compound of claim 28, wherein Y^3 is $-C(O)(CH_2)_4CH_3$.
30. The compound of claim 27, wherein Z^2 is $-OSi(CH_3)_2C(CH_3)_3$, $-OSi(PO_4)_2C(CH_3)_3$, $-C(O)CH_3$ or $-OC(O)CH_2CH_2CH_3$.
31. A pharmaceutical composition comprising the compound of claim 16.
32. A liposome having a bilayer comprising a lipid component, said lipid component comprising at least about 5 mole percent of the compound of claim 16.

5622001-16962460

 We hereby appoint the following attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Rosanne Goodman (Reg. No. 32,534) and Russell Lindenfeldar (Reg. No. 39,750) at The Liposome Company, Inc., One Research Way, Princeton, New Jersey, 08540, Telephone: (609) 452,7060, Telefax: (609) 734-0882. Address all correspondence to THE LIPOSOME COMPANY, INC. One Research Way, Princeton Forrestal Center, Princeton, NJ 08520.

The undersigned hereby authorize the U.S. attorneys named herein to accept and follow instructions from the undersigned assignee, if any, and/or, if the undersigned is not a resident of the United States, the undersigned's domestic attorney, patent attorney or patent agent, as to any action to be taken in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and the undersigned. In the even of a change in the person(s) from whom instructions may be taken, the U.S. attorneys named herein will be so notified by the undersigned.

The undersigned declare further that all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and

Further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

Date: _____

By: _____

Yong Wei

Date: _____

By: _____

Eric Mayhew

Date: _____

By: _____

Imran Ahmad

Date: _____

By: _____

Andrew S. Janoff

152424-162424

Applicant or Patentee: The Liposome Company, Inc.
Serial or Patent No.: 5,681,589
Filed or Issued: October 28, 1997
For: LIPOSOMAL CERAMIDE-RELATED COMPOUNDS AND THE
THERAPEUTIC USE THEREOF
Attorney's Docket No.: TLC - 144C

**VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(d) and 1.27(c) - SMALL BUSINESS CONCERN)**

I hereby declare that I am

- ☐ the owner of the small business concern identified below:
☒ an official of the small business concern empowered to act on behalf of the concern
identified below:

THE LIPOSOME COMPANY, INC.
One Research Way
Princeton Forrestal Center
Princeton, NJ 08540

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purpose of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties control or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled LIPOSOMAL CERAMIDE-RELATED COMPOUNDS AND THE THERAPEUTIC USE THEREOF by inventor(s) Yong Wei, Eric Mayhew, Imran Ahmad and Andrew Janoff., described in

- ☐ the specification filed herewith
☐ application serial no., _____ filed _____
☒ patent no. 5,681,589, issued October 28, 1997

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify

as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27).

NAME _____
ADDRESS _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT
ORGANIZATION

NAME _____
ADDRESS _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT
ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Michael McGrance
TITLE OF PERSON OTHER THAN OWNER Vice President and General Counsel
ADDRESS OF PERSON SIGNING The Liposome Company, Inc., 1 Research Way,
Princeton Forrestal Center, Princeton, New Jersey 08540

SIGNATURE  DATE October 25, 1999